

Intravascular Ultrasound Assessment of Atherosclerosis Progression and Regression

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Although angiography is still the most widely used method for definition of coronary anatomy, radiographic imaging depicts coronary anatomy as a simple two-dimensional projection of the lumen. There are many deficiencies inherent in this method for evaluating coronary disease¹. Available evidence demonstrates that a silhouette or "luminogram" is a relatively poor representation of coronary atheroma burden and a limited standard upon which to evaluate optimal therapy.

Measurement of the percent of stenosis represents the traditional method for characterizing angiographic lesion severity. This process requires comparison of luminal size within the lesion and an adjacent, uninvolved "normal" reference segment. However, necropsy studies demonstrate that coronary disease is frequently diffuse and contains no truly normal segment from which to calculate the percent area reduction. In the presence of diffuse disease, calculation of the percent of stenosis will predictably underestimate disease severity. In the most dramatic circumstances, diffuse, concentric, and symmetrical coronary disease affects the entire vessel, resulting in the angiographic appearance of a small, but normal artery.

Angiography is particularly confounded by the phenomenon of coronary "remodeling," first described in 1987 by Glagov². The remodeling process is observed histologically as the outward displacement of the external vessel wall in vascular segments with significant atherosclerosis. The adventitial enlargement opposes luminal encroachment thereby concealing the presence of the atheroma. Although such lesions do not restrict blood flow, clinical studies have demonstrated that the minimal or even unseen angiographic lesions represent the most important source for acute coronary syndromes, including myocardial infarction³.

The most salient example of the dissociation between quantitative angiography and clinical outcomes is provided by the literature on regression of atherosclerosis. A multitude of randomized lipid-lowering trials employed both angiographic and clinical assessment showing a negligible improvement of luminal caliber, typically an absolute difference of only 1-3%⁴. Yet these same studies yielded a large reduction in death and/or acute coronary events.

Coronary intravascular ultrasound provides valuable insights into the mechanisms underlying the dissociation between angiographic and clinical outcomes. Ultrasound commonly reveals atherosclerosis at coronary sites when no apparent disease is found by angiography⁵. Indeed, there may exist no segments free from atherosclerosis in some patients undergoing percutaneous coronary interventions. Because low-grade plaques are clearly implicated in acute coronary events, the extent of unrecognized atherosclerosis may determine the prognosis, not the degree of enlargement noted at the interventional site on the luminogram.

Several current studies are examining the application of intravascular ultrasound to the study of atherosclerosis progression or regression. Such studies offer the opportunity for important new insights into the disease process and the optimal means to reduce atherosclerotic burden.

(1) Topol EJ, **Nissen SE**: Our Preoccupation with Coronary Luminology. The Dissociation

Between Clinical and Angiographic Findings in Ischemic Heart Disease. *Circulation*, 1995;92:2333-2342.

(2) Glagov S, Weisenberg E, Zarins CK, Stankunavicius R, Kolettis GJ. Compensatory enlargement of human coronary arteries. *N Engl J Med* 316:1371-1375, 1987.

(3) Little WC, Constantinescu M, Applegate RJ, **et al.** Can arteriography predict the site of a subsequent myocardial infarction in patients with mild-to-moderate coronary artery disease? *Circulation* 78:1157-1166, 1988.

(4) Brown B, Zhao XQ, Sacco DE, Albers JJ. *Circulation*. Lipid lowering and plaque regression. New insights into prevention of plaque disruption and clinical events in coronary disease. *Circulation*. 1993;87:1781-1791.

(5) Tuzcu EM, Hobbs H, Rincon G , Bott-Silverman C , De Franco AC, Robinson K, McCarthy P, Stewart R, Guyer S, **Nissen SE:** Occult and Frequent Transmission of Atherosclerosis Coronary Disease with Cardia Transplantation.. *Circulation* 1995; 91: 1706-1713.